

Application Serial No. 09/988,013
Attorney Docket No. 40923-0048 US5

Listing of Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-24 (canceled).

25. (previously presented) A LL2 monoclonal antibody (mAb) or fragment thereof comprising complementarity-determining regions (CDRs) and framework (FR) regions, wherein the CDRs of the light chain variable region of said LL2 mAb comprise CDR1 comprising amino acids 24 to 40 of SEQ ID NO: 2, CDR2 comprising amino acids 56 to 62 of SEQ ID NO: 2 and CDR3 comprising 95 to 102 of SEQ ID NO: 2 and the CDRs of the heavy chain variable region of said LL2 mAb comprise CDR1 comprising amino acids 31 to 35 of SEQ ID NO: 4, CDR2 comprising amino acids 50 to 66 of SEQ ID NO: 4 and CDR3 comprising 99 to 105 of SEQ ID NO: 4.

26. (previously presented) The LL2 or fragment thereof of claim 25, further comprises:

- a) at least one FR of at least one light and heavy chain variable region of a human antibody;
- b) the light chain constant region and the heavy chain constant region of one or more human antibodies or
- c) a combination of a) and b)

27. (previously presented) The LL2 mAb or fragment thereof of claim 26, wherein said FRs of the light and heavy chain variable regions of said LL2 mAb comprise at least one amino acid substituted from said corresponding FRs of a murine LL2.

28. (Not entered) A method of designing an amino acid sequence of a variable domain of a humanized monoclonal antibody comprising:

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(a) determining residue identities between the amino acid sequences of a variable domain of a monoclonal antibody to be humanized and the corresponding variable domains of two or more human monoclonal antibodies using computer modeling;

(b) selecting framework regions from two or more of said corresponding variable domains wherein each framework region has a sequence identity of approximately 75.0 to 92.3% to the corresponding framework region in the monoclonal antibody to be humanized;

(c) incorporating the framework regions selected in step (b) with the complementarity determining regions of the monoclonal antibody to be humanized to design a humanized variable domain, wherein at least two of said framework regions are from different human monoclonal antibodies;

(d) retaining selected amino acid residues from the framework regions of the monoclonal antibody to be humanized in the corresponding framework regions of the humanized variable domain if one or more of said selected amino acids are predicted to have contacts with said complementarity determining regions affecting the affinity and specificity of the resultant humanized monoclonal antibody; and

(e) obtaining amino acid sequences of the variable domains of the light and heavy chain regions of the resultant humanized monoclonal antibody.

29. (Not entered) The method according to claim 28, wherein at least three of said framework regions are from different human monoclonal antibodies.

30. (Not entered) The method according to claim 28, wherein said framework regions are from the heavy chain region of different human monoclonal antibodies.

31. (Not entered) The method according to claim 28, wherein said selected amino acid residues of step (d) are within a 4.5 Angstrom radius of all atoms within each complementarity determining regions of the light and heavy chain of the resultant humanized monoclonal antibody.

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32. (Not entered) A method of producing a humanized monoclonal antibody designed according to the method of claim 28, comprising the additional steps of:

(f) preparing a DNA sequence encoding the variable domains of the resultant humanized monoclonal antibody based upon the designed amino acid sequence;

(g) operably incorporating the DNA sequences into at least one vector comprising the constant domains of the light and heavy chain regions;

(h) introducing the vector into a cell; and

(i) culturing the cell under conditions to produce the humanized monoclonal antibody.